January 14, 1953

Dear Dr. Cohn:

Your letter of December 1 was a tall order! I have been waiting for the supplementary message you promised, but have been able to recover my equilibrium somewhat meanwhile— enough to remind you about it. We do not have anything like the detailed physiological analysis of our mutants that would be needed to fill your specifications. I will do the best I can, but many of the stocks have to be repurified, checked, and put in some sort of order as wellaas, so far as possible, a uniform genotypic background so that the results will refer to known factors.

To go over some of the types in your requisition: Lac_3^- is the only thing even approaching a clearcut glucose-negative we have found (whether by isolations on glucose, lactose, or maltose). The point of block is somewhat mysterious (Mike had someone working on it). The genetics of Cst+ (constitutive Lac+) is still rather obscure; if it can be done, and when I can get to concentrate on it, I'll try to get the Cst+ Gal- combination by crossings. K-12 ferments melibiose poorly enough from the point of view of scoring on indicator agar that we've never gone after melibiose-negative mutants. We have some arabinose-negatives that have not been closely studied genetically, but you can have these anyhow. All Ara- have been Gal+, and vice versa. Of course, Ara- Gal- recombinants are not too difficult to get. [I assume you refer to l-arabinose]. The Lac- series is what I had in mind from the beginning. If you can let me know what you already have, and perhaps know, about this set, I will work up the others and send them on.

I have to admit that we have hardly begun the genetic analysis (not to mention physiology) of the fermentation mutants other than Lac-. The whole linkage system has had to be put into some sort of order before we could do a detailed analysis that would be meaningful. I think, however, that there are enough Lac- types, and enough genetic information on them to justify an immunogenetic study in your hands.

I hope you will always keep in mind the necessity of a close watch over the genotypic purity of the strains. Lac_3^-, for example, is always under considerable selective disadvantage as compared with a variety of reversions and suppressors that accumulate in almost any stock not closely watched. It would be unfortunate to be embarrassed by the difficulties that beset Mitchell et al. with tryptophane desmolase in Neurospora.

Yours sincerely,

Joshua Lederberg